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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,502	09/18/2001	Diana Downs	960296.97559	9804

27114 7590 12/22/2003

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EXAMINER

DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 12/22/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/955,502

Applicant(s)

DOWNS ET AL.

Examiner

Patricia A. Duffy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-15 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

The response filed 7-7-03 has been entered into the record.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-14 of this application. The provisional document does not provide conception and written description support for engineering or co-expression in the claimed subgenera of bacterial, yeast, mammalian or plant cells. Further, there is no conception of "using the protein". As such, the entire scope of the claimed invention lacks written description in the provisional document.

Drawings

The drawings have been approved by the draftsperson.

Information Disclosure Statement

No information disclosure statement has been filed in this application.

Election/Restrictions

Applicant's election of Group I, claims 1-14 in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)) and is hereby made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method of reducing superoxide damage to a cell comprising the step of engineering the cell to produce more than the native amount of the YggX protein or its homolog, wherein the cells are rendered more resistant to superoxide damage. The teachings of the specification are limited to a mutation in *S. enterica* called yggX*. This mutation is not described in chemical terms, nor does the specification teach the location of this mutation on the chromosome of *S. enterica* nor how it produces an increase in the native levels of YggX protein. The specification fails to describe engineering of the promoters, potential transactivators and repressors of the operon or gene sequence encoding any YggX protein or homolog thereof that leads to an increase in the expression of native YggX protein or its homolog. The specification teaches that the gene encoding the open reading frame of the native yggX and its yggX* mutant are identical (see page 13, last paragraph) and as such the mutation is not in the open reading frame but elsewhere in the chromosome and this mutation is not described. The

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description of the coding sequence of the open reading frames for YggX polypeptides or homologs in bacteria does not meet the description for the yggX* mutant and mutation of sequences that lead to an over expression of native YggX (i.e. the step of engineering the cell to produce more than the native amount of the YggX protein or its homology).

Additionally, Applicants admit that the art fails to describe any gene sequences for yggX in any archeal or eukaryotic genome sequences (page 14, second full paragraph). This specification fails to teach yggX gene sequences of yeast, mammalian, plants and archeal bacteria and therefore lack written description of engineering the cell to produce more than the native amount of the YggX protein or its homolog, because no homologs are known to exist in these cells and this specification fails to teach such. The written description is limited to yggX polypeptides and genes from eubacteria. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). The specification fails to teach the structure or relevant identifying characteristics of a representative number of "engineered" species resulting in the ability of a cell to produce more than the native amount of YggX protein or its homolog, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The recitation of "YggX" or homolog thereof does not

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convey a common structure or function. The scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure and the claims. With the exception of native sequences comprising SEQ ID NO:1, no common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Applicants were not in possession of the claimed genus because the specification does not convey to one of skill in the art a representative number of variants in structure and function of any such polypeptide that has the claimed structure and function. The genus of polypeptides with the claimed function is substantial and highly variant because the polypeptides do not have a common structure and function. The recitation of "YggX" does not convey a common structure nor a common function. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant and not conveyed by way of written description by the specification at the time of filing. As such the specification lacks written description for the highly variant genus of single function polypeptides and one skilled in the art would not recognize that applicants had possession of the genus of genes encoding YggX polypeptides or homologs thereof for use in the method. As such, the written description is limited to methods that reduce superoxide damage to an eubacterial cell comprising vector-based overexpression of the endogenous yggX gene from said cell, wherein said overexpression renders the cells more resistant to superoxide damage.

Claims 9-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in

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the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method of increasing resistance of an oxygen-labile protein to oxidative damage, comprising the step of co-expressing the oxygen-labile protein with the YggX protein or a homolog in a host cell. The teachings of the specification are limited to increasing the resistance to oxidative damage of enzymes having an oxygen labile Fe-S cluster/center. The specification fails to teach describe other oxygen-labile polypeptides or proteins that have reduced oxidative damage or any means to determine the oxidative damage of such. The specification fails to provide any written description of how to examine oxygen-labile proteins for the amount of oxidative damage as it relates to claim 10. The specification does not teach any oxygen-labile proteins that are not bacterial enzymes having an oxygen labile Fe-S cluster/center which have increased resistance to oxidative damage in the presence of YggX. The description of the coding sequence of the open reading frames for native YggX polypeptides comprising SEQ ID NO:1 in eubacteria does not meet the description for homologous sequences in cells. Applicants admit that the art fails to describe any gene sequences for yggX in any archeal or eukaryotic genome sequences (page 14, second full paragraph). This specification fails to teach yggX gene sequences of yeast, mammalian, plants and archeal bacteria and therefor lack written description of co-expressing these or claimed homologs, because no homologs are known to exist in these cells and this specification fails to teach such. The written description is limited to yggX polypeptides and corresponding genes from eubacteria and bacterial enzymes having an oxygen labile Fe-S center. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented

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what is claimed." (See Vas-Cath at page 1116.). The specification fails to teach the structure or relevant identifying characteristics of a representative number of "oxygen-labile protein" and YggX proteins or homologs resulting in the ability of increasing the resistance of an oxygen-labile protein a host cell, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The recitation of "YggX" or homolog thereof does not convey a common structure or function. The scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure and the claims. With the exception of native sequences comprising SEQ ID NO:1, no common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Applicants were not in possession of the claimed genus because the specification does not convey to one of skill in the art a representative number of variants in structure and function of any such polypeptide that has the claimed/structure and function. The genus of polypeptides with the claimed function is substantial and highly variant because the polypeptides do not have a common structure and function. The recitation of "YggX" does not convey a common structure nor a common function. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant and not conveyed by way of written description by the

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specification at the time of filing. As such the specification lacks written description for the highly variant genus of single function polypeptides and one skilled in the art would not recognize that applicants had possession of the genus of genes encoding YggX polypeptides or homologs thereof or oxygen-labile polypeptides for use in the method. As such, the written description is limited to methods of increasing the resistance of a bacterial enzyme having an oxygen labile Fe-S cluster/center to oxidative damage comprising co-expressing the bacterial enzyme having the oxygen labile Fe-S cluster/center with a native YggX polypeptide in a eubacterial cell.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 1-8, the claims are indefinite from the use of the term "engineering the cell". "Engineering" is not an art defined term and the metes and bounds of such is not defined by the specification. As to claims 7 and 8, the term "protein is used" or "protein homolog is used" renders the claims indefinite because it is unclear how the protein is "used" or how this relates to "engineering". As to claim 2, this claim is not logically dependent from claim 1, because if the step of engineering the cell to produce more than the native amount to the YggX protein or its homolog does not render the cell more resistant to superoxide damage, then method of claim 1 can not in fact be practiced. Either the cells are rendered more resistant to superoxide damage by the step of claim 1 or they are not. As such, it is unclear what the intent of this additional step is in claim 2 and how it provides for a method of reducing superoxide damage to a cell as recited in the preamble of claim 1.

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As to claims 1-14, independent claim the recitation of "the YggX" lacks internal antecedent basis. This issue is easily resolved by Applicants amending the claims to recite -- ...with a YggX protein...- .

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

It is noted that the provisional document does not provide written description support and enablement for the scope of the claimed invention for reasons set forth in the priority section above. Therefore, the prior art date is the instant filing date of 9/18/01.

Claims 1, 2, 3, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Gralnick et al (Abstracts of the General meeting of the American Society for Microbiology, 100p441, May 21-25, 2000.

Gralnick et al teach the use of yggX as a general suppressor of gshA mutants in Salmonella. As such, Gralnick et al anticipates the claimed invention.

Claims 1, 2, 3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Pianzola et al (Journal of Bacteriology 178(23):6736-6742, 1996.

Pianzola et al teach the overexpression of the rbo gene product in a superoxide dismutase deficient Escherichia coli suppressed all deleterious effects of superoxide

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deficiency in *Escherichia coli*, including inactivation by superoxide enzymes containing 4Fe-4S clusters and DNA damage produced via the superoxide-enhanced Fenton reaction. In *Escherichia coli*, rho may permit the bacterium to avoid superoxide stress by maintaining superoxide stress (i.e. the instant superoxide damage) by maintaining functional (reduced) superoxide sensitive 4Fe-4S clusters. Pianzzola et al therefore teaches methods of reducing superoxide damage to a cell (i.e. inactivation of 4Fe-4S clusters and DNA damage) by the overexpression of the rbo gene product of *Desulfoarculus baarsii* in a superoxide dismutase deficient *Escherichia coli* (see abstract).

In view of the lack of structure for YggX and homologs as recited in the claims and in view that the rbo gene product functions the same, it meets the limitation of YggX protein or its homolog. The recitation of YggX in the claim does not patentably distinguish the methods from other methods using differently named proteins that have the same effect.

Claims 1, 2, 4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Portnoy et al (*Journal of Biological Chemistry*, 274(21):15041-15045, 1999).

Portnoy et al teach the overproduction of *Saccharomyces cerevisiae* Atx1p. The overproduction of Atx1p in *Saccharomyces cerevisiae* mutants (i.e. the instantly claimed yeasts) substitutes for superoxide dismutase 1 in preventing oxidative damage (see abstract and Figure 4).

In view of the lack of structure for YggX and homologs as recited in the claims and in view that the Atx1p gene product functions the same, it meets the limitation of YggX protein or its homolog. The recitation of "YggX" does not structurally distinguish nor patentably distinguish the methods from other methods using differently named proteins that have the same effect.

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Claims 1, 2, 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Kelner et al (Journal of Biological Chemistry, 275(1):580-584, 2000).

Kelner et al teaches protein/gene Atox1 that suppresses oxidative damage in yeast lacking superoxide dismutase. Atox1 was shown to protect superoxide dismutase deficient yeast from oxidative damage induced by superoxide anions and hydrogen peroxide (page 580, column 2, first full paragraph). Kelner et al teach that the transfection into several neuronal cell lines to increase the endogenous level of Atox1 expression have demonstrated that the transfected neurons (i.e. the instantly claimed mammalian cells) are significantly protected against this oxidative stress (see abstract, page 582 paragraph bridging columns 1-2). Atox1 has the ability to suppressive oxidative damage by superoxide. As such, Kelner et al anticipates the claimed invention.

In view of the lack of structure for YggX and homologs as recited in the claims and in view that the Atox1 gene product functions the same, it meets the limitation of YggX protein or its homolog. The recitation of "YggX" does not structurally distinguish nor patentably distinguish the methods from other methods using differently named proteins that have the same effect.

Claims 1, 2, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Ben-Amor et al (Plant Cell and Environment, 22(12):1579-1586, 1999).

Ben-Amor et al teach the use of an antisense ACC oxidase (ACO) gene reduced the sensitivity of cantaloupe melons to chilling injury and severe chilling injury correlated with a lower activity of activated oxygen scavenging enzymes. Ben-Amor et al teach that the tolerance to chilling was associated with a lower accumulation of ethanol, acetaldehyde, reduced membrane deterioration and higher capacity of the fruit to remove active oxygen species (i.e. superoxide and hydrogen peroxide). Ben-Amor et al teach that the antisense treatment (i.e. the instant engineering) provides for an increase in the activities of catalase, superoxide dismutase and peroxidase, the preeminent enzymes that reduce

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reactive oxygen species such as superoxide. Ben-Amor et al teach that severe chilling injury was correlated with a lower activity of activated oxygen scavenging enzymes and that increasing these enzymes leads to chilling tolerance which necessarily and inherently results from reducing superoxide damage to the plant cells by means of increasing in the activities of catalase, superoxide dismutase and peroxidase (see abstract). Ben-Amor et al therefore anticipates the claimed invention.

In view of the lack of structure for YggX and homologs as recited in the claims and in view that the antisense gene product functions to increase activities of catalase, superoxide dismutase and peroxidase, it meets the limitation of YggX protein or its homolog. The recitation of "YggX" does not structurally distinguish nor patentably distinguish the methods from other methods using differently "engineered" proteins that have the same effect.

Status of the Claims

Claims 1-14 stand rejected. Claim 15 is withdrawn from consideration.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 703-305-7555. After January 27, 2004, the telephone for the examiner will change to 571-272-0855. The examiner can normally be reached on M-F 9:30pm-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Smith Lynette can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patricia A. Duffy
Patricia A. Duffy, Ph.D.

Primary Examiner

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